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EXAMINER	
STEADMAN, DAVID J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,752	IKEDA, KEIKO	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-13* is/are pending in the application.

4a) Of the above claim(s) *5 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/08 has been entered.

[2] Claims 1 and 3-13 are pending in the application.

[3] Applicant's amendment to the claims, filed on 9/22/08, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicant's arguments filed on 9/22/08 in response to the Office communications mailed on 5/29/08 and 9/12/08 have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[6] Applicant continues to traverse the restriction requirement on the grounds that the inventions of Groups I and II share the same special technical feature, which feature is a contribution over the prior art.

Applicant's argument is not found persuasive. According to PCT Rule 13.2 unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. At least for the reasons set forth below, the examiner maintains the position that the technical feature of Group I is not a contribution over the prior art and thus the inventions of Groups I and II do not have unity of invention.

[7] Claims 5 and 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/9/07.

[8] Claims 1, 3-4, 6-10, and 12-13 are being examined on the merits.

Priority

[9] As noted in a prior Office action, applicant's claim to foreign priority under 35 USC § 119(a)-(d) to Japanese application JP 2003-005099, filed on 1/10/03, is acknowledged. A certified copy of the foreign priority document has been filed in the instant application on 7/8/05. The priority claim is set forth in the Declaration filed under 37 CFR 1.63 on 2/7/06.

Claim Objection

[10] Claim 1 is objected to in the recitation of "…cytoplasmic polyhedrosis is…" and in order to improve claim form, it is suggested that the noted phrase be amended to recite, "…cytoplasmic polyhedrosis virus is…"

Claim Rejections - 35 USC § 112, Second Paragraph

[11] Claims 1, 3-4, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (claims 3-4, 6-8, 10, and 12-13 dependent therefrom) is indefinite in the recitation of "…capsid protein VP3…a region from the 41st amino acid residue to the 79th amino acid residue…" because it is unclear from the claims and the specification as to the reference sequence(s) to which the amino acid numbering refers. The amino acid numbering presumably refers to a *specific* sequence, which, according to the claims and specification is critical to interacting with a polyhedral protein. It is suggested that, *e.g.,* the claim be amended to recite a particular reference sequence by use of a sequence identifier, *i.e.,* "SEQ ID NO:".

Claim Rejections - 35 USC § 112, First Paragraph

[12] Claims 1, 3-4, 6-10, and 12-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

According to MPEP 2163.II.A.1, in evaluating a claimed invention for adequate written description, the examiner should determine what the claim as a whole covers. "Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997)."

The claims recite a genus of protein complexes comprising any polyhedral protein having an insect virus encapsulated therein and a target protein having a "restricted region" of a *B. mori* CPV strain H VP3 capsid protein as an embedding signal, the "restricted region" being limited in claim 1 to amino acids 41-79.

In view of the recitation of the grammatically indefinite article "a" in the phrase "a region from the 41st amino acid residue to the 79th amino acid residue", the phrase has been broadly, but reasonably interpreted as any two contiguous amino acid sequence of a *B. mori* CPV strain H VP3 protein.

Although claims 6 and 9 do not specify which amino acids are intended as being a "restricted region", the specification defines "restricted region" as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue of a capsid protein VP3 of cytoplasmic polyhedrosis virus" (p. 6, second paragraph). "Where an explicit definition is provided by

the applicant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999)".

MPEP 2163.II.A.2.(a).i) states, "Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention".

The specification discloses the reduction to practice of a single representative species of the genus of recited protein complexes, *i.e.,* a protein complex of a *B. mori* CPV strain H polyhedral protein having an encapsulated *B. mori* CPV strain H and a target protein fused to the C-terminus of amino acids 41 to 79 of *Bombyx mori* CPV strain H VP3 protein as disclosed by Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF). There are no other drawings or structural formulas disclosing a protein complex as encompassed by the claims and other than interaction requiring *B. mori* polyhedrin and amino acids 41-79 of *B. mori* CPV strain H VP3 protein as disclosed by Ohta et al. (*supra*), there is no prior-art or disclosed teaching regarding interaction between *any* polyhedral protein and amino acids 1-40 or amino acids 41-79 of *B. mori* CPV strain H VP3 protein. According to the reference of Ikeda et al.

(reference AN of the IDS filed on 7/8/05), "little is known about the specific interactions between CPV polyhedron and the viral capsid protein," particularly the interaction between CPV polyhedron and VP3 (p. 994, column 1, middle). Thus, other than the interaction between BmCPV strain H polyhedrin and VP3, there is no way to predict interaction of any VP3 protein of any strain of *Bombyx mori* CPV with any other strain of *B. mori* CPV polyhedrin to achieve a protein complex as encompassed by the claims. Furthermore, it is noted that even after the time of the invention, the reference of Mori et al. (*J. Biol. Chem.* 282:1728917296, 2007; cited in the PTO-892 mailed on 12/20/07), in disclosing production of *B. mori* CPV polyhedra containing human FGF-2, teaches that "only degradation products of FGF-2 were found in polyhedra where FGF-2 was fused with VP3 at the N terminus" (p. 17292, column 1, first paragraph).

Given what is disclosed in the art regarding interaction between a polyhedral protein and a VP3 protein, and given the absence of a disclosed correlation between structure and function, the specification, taken with the pre-existing and post-filing art regarding of polyhedral protein and VP3 protein interaction, fails to satisfy the written description requirement of 35 U.S.C. 112, first paragraph.

[13] Claim(s) 1, 3-4, 6-10, and 12-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein complex of a *Bombyx mori* CPV strain H polyhedral protein having an encapsulated *Bombyx mori* CPV strain H and a target protein fused to the C-terminus of amino acids 41 to 79 of *Bombyx mori* CPV strain H VP3 protein as disclosed by Ohta et al. (WO 02/36785; cited

in the IDS filed on 7/8/05 as reference AF), does not reasonably provide enablement for all protein complexes as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors considered to be most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: Claim 1 (claims 3-4 dependent therefrom) is drawn to an isolated protein complex comprising the following moieties: 1) a polyhedral protein having an insect virus encapsulated therein and 2) a target protein fused to a restricted region of a *B. mori* CPV strain H VP3 capsid protein, wherein the restricted region is

amino acids 41 to 79. The source of the polyhedral protein is unlimited. The fusion between the target protein and the restricted region has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion, at either the N- and/or C-terminus. In view of the recitation of the grammatically indefinite article “a” in the phrase “a region from the 41st amino acid residue to the 79th amino acid residue”, the phrase has been broadly, but reasonably interpreted as any two contiguous amino acid sequence of a *B. mori* CPV strain H VP3 protein.

Claim 6 (claims 7-8 dependent therefrom) is drawn to a biosensor comprising an isolated protein complex comprising the following moieties: 1) a polyhedral protein having an insect virus encapsulated therein and 2) a target protein fused to a restricted region of a *B. mori* CPV strain H VP3 capsid protein, wherein the protein complex is arranged in dots or lines on a substrate and immobilized thereon. Similar to the interpretation of claim 1, the source of the polyhedral protein is unlimited and there is no limitation in claim 6 that requires the *direct* fusion between the target protein and the restricted region and the term “fused” has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion at either the N- and/or C-terminus. Although claim 6 does not specify which amino acids are intended as being a "restricted region", the specification defines “restricted region” as “either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue of a capsid protein VP3 of cytoplasmic polyhedrosis virus” (p. 6, second paragraph).

Claim 9 is drawn to an isolated protein complex comprising the following moieties: 1) a polyhedral protein having an insect virus encapsulated therein and 2) a target protein fused to a restricted region of a *B. mori* CPV strain H VP3 capsid protein, wherein the target protein is an enzyme. Similar to the interpretation of claims 1 and 6, the source of the polyhedral protein is unlimited and there is no limitation in claim 9 that requires the *direct* fusion between the target protein and the restricted region and the term "fused" has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion at either the N- and/or C-terminus. As with claim 6, although claim 9 does not specify which amino acids are intended as being a "restricted region", the specification defines "restricted region" as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue of a capsid protein VP3 of cytoplasmic polyhedrosis virus" (p. 6, second paragraph).

Claims 10 and 12-13 require the target protein to be directly fused to the restricted region, however, there is no claim limitation that requires the target protein be heterologous to the restricted region and thus the target protein can be considered to be a part of the VP3 protein itself, *e.g.,* amino acids 1-40 or 80-1057.

The state of the prior art; The level of one of ordinary skill; The level of predictability in the art: Protein complexes of a target protein occluded by the polyhedra of *nuclear* polyhedrosis viruses are well-known in the prior art. However, application of this concept to other viruses, *e.g.,* CPVs, appears to require knowledge of those regions of the polyhedra that are non-essential for crystallization and interactions between the

proteins of the polyhedron and proteins occluded thereby. In this case, Ikeda et al. (*supra*) and Ohta et al. (*supra*) discloses a sequence of a BmCPV H strain VP3 polypeptide (SEQ ID NO:2) that is able to be occluded by the BmCPV H strain polyhedron. However, the prior art does not appear to characterize this interaction between any other polyhedral proteins and a BmCPV H strain VP3 polypeptide as broadly encompassed by the claims. As noted in Ikeda et al. (*supra*), "little is known about the specific interactions between CPV polyhedron and the viral capsid protein," particularly the interaction between CPV polyhedron and VP3 (p. 994, column 1, middle). Thus, other than the interaction between BmCPV strain H polyhedrin and VP3, there is no way to predict interaction of any VP3 protein of any strain of *Bombyx mori* CPV with any other strain of *B. mori* CPV polyhedrin to achieve a protein complex as encompassed by the claims. Furthermore, it is noted that the post-filing reference of Mori et al. (*supra*), in disclosing production of *B. mori* CPV polyhedra containing human FGF-2, teaches that "only degradation products of FGF-2 were found in polyhedra where FGF-2 was fused with VP3 at the N terminus" (p. 17292, column 1, first paragraph).

The amount of direction provided by the inventor; The existence of working examples: The specification's working examples of the claimed protein complex is a protein complex of a target protein fused to the C-terminus of at least BmCPV strain H VP3 amino acids 1-79 embedded within the BmCPV strain H polyhedrin. Other than this working example, the specification fails to provide the necessary specific guidance for making other protein complexes as encompassed by the claims.

Also, as noted above, the specification defines "restricted region" as "either a region from the N-terminus to the 40th amino acid residue or the region from the 41st amino acid residue to the 79th amino acid residue of a capsid protein VP3 of cytoplasmic polyhedrosis virus" (p. 6, second paragraph). According to the specification, C-terminal deletions of VP3 up to amino acid 39 actually *disrupt* immobilization of a target protein into polyhedra (Figure 3) as compared to a VP3 with amino acids 1 to 79.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the state of the art regarding interaction between viral polyhedrin and CPV VP3 proteins, and the high level of unpredictability as noted above, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

RESPONSE TO ARGUMENT: At p. 7 of the instant remarks, applicant argues the rejection is obviated by amendment to limit the VP3 protein to *B. mori* CPV strain H VP3.

Applicant's argument is not found persuasive. At least for the reasons stated above in the detailed analysis of the Factors of *In re Wands,* the examiner maintains the position that the specification fails to describe and enable all protein complexes as encompassed by the claims.

Claim Rejections - 35 USC § 102/103

[14] Claim(s) 1, 3-4, 9-10, and 13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ohta et al. (WO 02/36785; cited in the IDS filed on 7/8/05 as reference AF; "Ohta"). Since the Ohta reference is a non-English language document, reference to the corresponding US Patent Application Publication 2004/0059091 (cited in the IDS filed on 7/8/05 as reference AA) will be used as an English-language equivalent of the Ohta reference, particularly as the IDS filed on 7/8/05 indicates that US Patent Application Publication 2004/0059091 is a translation of the Ohta reference. See MPEP 2112.III regarding a rejection under 35 U.S.C. 102/103.

CLAIM INTERPRETATION: The following comments are provided in order to clarify the examiner's broadest reasonable interpretation of the claims. Claim 1 is drawn to an isolated protein complex comprising the following moieties: 1) a polyhedral protein having an insect virus encapsulated therein and 2) a target protein fused to a restricted

region of a *B. mori* CPV strain H VP3 capsid protein, wherein the restricted region is from amino acid 41 to 79. Claim 9 is similar to claim 1 but without specifying the amino acids of the restricted region. The fusion between the target protein and the restricted region has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion.

Claims 10 and 13 require the target protein to be directly fused to the restricted region, however, there is no claim limitation that requires the target protein be heterologous to the restricted region and thus the target protein can be considered to be a part of the VP3 protein itself.

The reference of Ohta teaches a protein complex of *B. mori* CPV (BmCPV) strain H polyhedra with occluded BmCPV VP3 fused to GFP (p. 8, paragraph 110). According to Ohta, "It has been demonstrated that virions enter specifically into the polyhedra because of the specific relation between the viral occlusion body protein of virions and polyhedrin" (p. 1, paragraph 17), thus, although Ohta does not expressly teach the protein complex has an encapsulated virion(s), this would be a necessary feature of the protein complex of Ohta. Also, although Ohta does not teach the BmCPV strain H VP3 of the VP3-GFP chimeric protein has a "restricted region…as an embedding signal for polyhedron", since the chimeric protein of Ohta has an intact N-terminus and is occluded by the BmCPV strain H polyhedra (*e.g.,* p. 8, paragraph 104), one of ordinary skill in the art would recognize that the VP3 of the chimeric protein of Ohta necessarily has such a "restricted region". This anticipates claim 1 when the target protein is interpreted as being indirectly fused to the restricted region and this anticipates claim 10

when any amino acid sequence directly adjacent to amino acids 41 to 79 of the VP3 protein of Ohta, *e.g.,* amino acids 1-40 or 80-1057, are interpreted as being a "target protein".

Ohta teaches the objective protein can be an enzyme, which anticipates claims 4, 9, and 10.

Ohta teaches, "the protein complex…with the objective protein occluded with polyhedrin…where polyhedrin contributes to improvement of stability, or protection, or improvement of preservability of the objective protein, or combination thereof" (p. 2, paragraph 23), which anticipates claim 3.

RESPONSE TO ARGUMENT: Beginning at p. 8 of the instant remarks, applicant argues Ohta discloses fusing a target protein to a complete VP3 protein, not a restricted region of residues 41 to 79 and thus does not teach all claim limitations.

Applicant's argument is not found persuasive. As noted above, there is no limitation in claims 1 and 9 that requires the *direct* fusion between the target protein and the restricted region and the term "fused" has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion. While it is acknowledged that claims 10 and 13 require the target protein to be directly fused to the restricted region, there is no claim limitation that requires the target protein be heterologous to the restricted region and thus the "target protein" can be broadly but reasonably interpreted to be a part of the VP3 protein itself, *e.g.,* amino acids 1-40 or

80-1057. As such, the examiner maintains the position that the reference of Ohta teaches – either explicitly or inherently – all limitations of the claims.

Beginning at p. 10 of the instant remarks, applicant argues one cannot interpret the claims as an indirect fusion because "The recitation of a 'restricted region'…requires that the restricted region has been excised from the full protein…the 'restricted region' requires that amino acids 40 and 41…have been 'cut' from each other" (paragraph bridging pp. 10-11). However, the examiner can find no specific definition in the specification or a claim limitation that requires such a narrow interpretation of the claims. As such, the features upon which applicant relies (i.e., amino acids 40 and 41 have been cut from each other) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). If applicant intends for the claims to require that amino acid 41 of VP3 be "cut" from amino acid 40, it is suggested that applicant amend the claims to define the "restricted region" to require such a limitation. "Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified" (MPEP 2111).

Claim Rejections - 35 USC § 103

[15] Claim(s) 6-8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohta (*supra*) in view of Hosokawa et al. (Materials Research Society, Symposium

C, Bio-Inspired Nanoscale Hybrid Systems, December 2002, Abstract C3.5; available at www.mrs.org/s_mrs/bin.asp?CID=2109&DID=91203&DOC=FILE.PDF; cited in the PTO-892 mailed on 12/20/07; "Hosokawa") and Ito et al. (*Appl. Physics Lett.* 78:2566-2568, 2001; cited in the PTO-892 mailed on 12/20/07; "Ito").

CLAIM INTERPRETATION: Claim 6 is drawn to a biosensor comprising an isolated protein complex comprising the following moieties: 1) a polyhedral protein having an insect virus encapsulated therein and 2) a target protein fused to a restricted region of a *B. mori* CPV strain H VP3 capsid protein, wherein the protein complex is arranged in dots or lines on a substrate and immobilized thereon. Similar to the interpretation of claim 9, there is no limitation in claim 6 that requires the *direct* fusion between the target protein and the restricted region and the term "fused" has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion. While it is acknowledged that claim 12 requires the target protein to be directly fused to the restricted region, there is no claim limitation that requires the target protein be heterologous to the restricted region and thus the "target protein" can be broadly but reasonably interpreted to be a part of the VP3 protein itself, *e.g.,* amino acids 1-40 or 80-1057.

Claim 7 limits the protein complex of claim 6 to being "packed in such a manner that said isolated protein complex is to be contacted with a substance in a test solution in a recess formed on a substrate". The limitation "is to be contacted..." has been broadly, but reasonably interpreted as an intended use of the protein complex, the claim being interpreted as requiring only that the protein complex be "packed" in a manner

suitable for being contacted with a substance in a test solution in a recess formed on a substrate, but not actively requiring the protein complex be in contact with a substance in a test solution in a recess formed on a substrate.

Claim 8 limits the protein complex of claim 6 to being packed in a container in such a manner that said isolated protein complex is to be contacted with a substance in a test solution. Similar to claim 7, the limitation "is to be contacted..." has been broadly, but reasonably interpreted as an intended use of the protein complex, the claim being interpreted as requiring only that the protein complex be “packed in a container” in a manner *suitable for* being contacted with a substance in a test solution, but not actively requiring the protein complex be in contact with a substance in a test solution. The term “container” has been broadly, but reasonably interpreted as an object that holds the protein complex or to which the protein complex is affixed.

The reference of Ohta teaches a protein complex as noted above. Ohta does not teach a biosensor comprising the protein complex, wherein the protein complex is arranged in dots or lines on a substrate and immobilized thereon.

The reference of Hosokawa teaches, “The proteomics technique has received significant attention as an important technique for disease diagnosis and for monitoring drug efficacy and safety. To realize the high-throughput analysis of proteins expression, preparation of protein microarrays is strongly requested, however, it is very difficult in comparison with DNA microarrays because of complex structures of proteins. Recently, we have been interested in applying protein crystal of polyhedra, which are μm-size proteinaceous occlusion bodies produced by insect viruses, for immobilization of

functional proteins. On the other hand, a laser trapping technique based on the photon pressure has received much attention as a technique to manipulate biocells and microparticles. Recently, furthermore, we have already succeeded photothermal fixation of polymer microparticles onto a polymer substrate by local heating due to UV laser irradiation. It is considered that the polyhedra crystals are very useful to fabricate protein microarrays and we demonstrated here that the polyhedra crystals of a few μm could be fixed one by one on a slide glass by laser manipulation technique. Aqueous solution containing the dispersed polyhedra crystals was set on the microscope stage and each crystal was trapped by a focused 1064 nm beam of a Nd^{3+} : YAG laser. On the trapped polyhedra, femtosecond laser was irradiated to fix it on a polymer substrate. Damages of the polyhedra crystals will be decreased by adjusting femtosecond laser and noncontact pattering of the polyhedra crystal is realized with the precision less than 1 μm".

Ito discloses a method for fixing nanoparticles onto a glass substrate using a 1064 nm Nd^{3+} : YAG laser (pp. 2566-2567), wherein the nanoparticles comprise a fluorescent dye (2566, column 2), and the nanoparticles are placed onto the glass substrate in a dot or a line (p. 2567, Figures 1-3). Ito further teaches "The present method will be extended" to "hopefully" fix "biological molecules" (p. 2568, column 1).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Ohta, Hosokawa, and Ito for a protein microarray of the protein complex of Ohta affixed to a glass substrate in dots or lines. One would have been motivated to do this because Hosokawa expressly teach doing this using a

polyhedra crystal and the protein complex of Ohta, having an embedded GFP, would have provided a means for monitoring whether or not the protein crystal was fixed to the glass substrate, and Ito, which teaches fixing the fluorescent nanoparticles in dots or lines as noted above. One would have a reasonable expectation of success for a protein microarray of the protein complex of Ohta affixed to a glass substrate according to the methods of Hosokawa and Ito because of the results of Ohta, Hosokawa, and Ito. Therefore, claims 6-8 and 12, drawn to a biosensor as described above would have been obvious to one of ordinary skill in the art at the time of the invention.

RESPONSE TO ARGUMENT: Applicant argues the references of Hosokawa and Ito fail to remedy the alleged deficiencies of Ohta. However, this is not found persuasive in view of a broad, but reasonable interpretation of the claims in combination with the relevant teachings of Ohta, Hosokawa, and Ito as noted above.

Claim Rejections – Double Patenting

[16] Claims 1, 3-4, 9-10, and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of US Patent 7,432,347 ("'347 patent").

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 3-4, 9-10, and 13 of the instant application are generic to all that is recited in claims 1-6 of the '347 patent in view of a broad, but reasonable interpretation as noted above, i.e., claims 1, 3-4, 9-10, and 13 of the instant application are anticipated by claims 1-6 of the '347 patent.

[17] Claims 6-8 and 12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of the '347 patent in view of Hosokawa (*supra*) and Ito (*supra*).

Although the claims of the '347 patent do not recite a "biosensor", such a biosensor would have been obvious in view of the relevant teachings of Hosokawa and Ito as noted above. One would have been motivated to make such a biosensor because Hosokawa expressly teaches doing this using a polyhedra crystal and the protein complex of the '347 patent, having an embedded GFP, would have provided a means for monitoring whether or not the protein crystal was fixed to the glass substrate, and Ito, which teaches fixing the fluorescent nanoparticles in dots or lines as noted above. One would have had a reasonable expectation of success for a protein microarray of the protein complex as claimed by the '347 patent affixed to a glass substrate according to the methods of Hosokawa and Ito because of the results of Hosokawa, and Ito.

RESPONSE TO ARGUMENT: Applicant argues the claimed invention is patentably distinguished over the '347 patent (referred to as "Ohta" by applicant) because the '347 patent does not disclose fusing a target protein to a restricted region of residues 41 to 79.

Applicant's argument is not found persuasive. As noted above, there is no limitation in claims 1 and 9 herein that requires the *direct* fusion between the target protein and the restricted region and the term "fused" has been interpreted in accordance with MPEP 2111 as being both a *direct* fusion and an *indirect* fusion. While it is acknowledged that claims 10 and 13 require the target protein to be directly fused to the restricted region, there is no claim limitation that requires the target protein be heterologous to the restricted region and thus the "target protein" can be broadly but reasonably interpreted to be a part of the VP3 protein itself, *e.g.,* amino acids 1-40 or 80-1057. As such, the examiner maintains the position that the reference of Ohta teaches – either explicitly or inherently – all limitations of the claims.

Beginning at p. 10 of the instant remarks, applicant argues one cannot interpret the claims as an indirect fusion because "The recitation of a 'restricted region'…requires that the restricted region has been excised from the full protein…the 'restricted region' requires that amino acids 40 and 41…have been 'cut' from each other" (paragraph bridging pp. 10-11). However, the examiner can find no specific definition in the specification or a claim limitation that requires such a narrow interpretation of the claims. As such, the features upon which applicant relies (i.e., amino acids 40 and 41 have been cut from each other) are not recited in the rejected claim(s). Although the

claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). If applicant intends for the claims to require that amino acid 41 of VP3 be "cut" from amino acid 40, it is suggested that applicant amend the claims to define the "restricted region" to require such a limitation. "Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified" (MPEP 2111).

Conclusion

[18] Status of the claims:

- Claims 1 and 3-13 are pending.
- Claims 5 and 11 are withdrawn from consideration.
- Claims 1, 3-4, 6-10, and 12-13 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/
Primary Examiner, Art Unit 1656